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Effects of Simulated Shift Schedules on Visual Search

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between sleep loss phenotypes and cognition in FXS mice (Fmr1 KO). We hypothesized that normalizing sleep in Fmr1 KO mice could improve sleep-dependent cognitive function. Because direct activation of G-protein inward rectifying potassium (GIRK) channels by ML297 has been found to promote NREM sleep, we tested how ML297 affected sleep and memory consolidation phenotypes in Fmr1 KO mice. **Methods:** Wild type (WT) and Fmr1 KO were implanted with electrodes for electroencephalogram/electromyogram (EEG/EMG) recording of wakefulness, NREM and REM sleep. Sleep-dependent memory consolidation was measured using single-trial contextual fear conditioning (CFC). ML297 or vehicle was administered after CFC training to measure the effects on sleep and fear memory consolidation.

Results: Fmr1 KO mice showed reduced sleep in the hours following CFC learning compared to wild type littermates, and reduced contextual fear memory consolidation. Post-CFC sleep deprivation disrupted memory consolidation in wild type littermates, but not Fmr1 KO mice. Both NREM sleep time and NREM bout length were reduced in Fmr1 KO mice, and preliminary data suggest reduced NREM delta (0.5–4 Hz) power in the prefrontal cortex. These deficits were present at baseline and also following CFC. Post-CFC training administration of ML297 rescued NREM sleep and contextual fear memory deficits in Fmr1 KO mice.

Conclusion: Our study showed a strong link between NREM sleep loss and cognitive deficits in Fmr1 KO mice. Critically, normalization of NREM sleep through direct activation of GIRK channels rescues cognitive deficits seen in Fmr1 KO mice, suggesting a new therapeutic approach to treating cognitive deficits associated with FXS.

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055

NOVEL SLEEP-DEPENDENT SPATIAL MEMORY AND NAVIGATION TASK USING MINECRAFT

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Introduction: Spatial navigation and memory are hippocampally-dependent and decrease with age, yet, ecologically-valid methods remain elusive. We developed an engaging and inherently flexible spatial navigation/memory task using the Minecraft platform to test sleep-dependent memory. We validated baseline performance and learning rates across two separate Minecraft environments.

Methods: Using a within-subjects design, twenty-two subjects experienced two conditions (wake/sleep) and two Minecraft environments, counterbalanced across subjects. At encoding, subjects learned the locations of 12 objects. Memory for object location accuracy and navigation route (distance between start and target; vector: angle of direction towards target location from start) was tested immediately and following 12-hours of wake or sleep. Post-hoc analyses were conducted using a median split on subjects' Immediate test performance.

Results: There were no significant differences across conditions for the Immediate test performance ($t(22) = .567, p = .576$) across the two environments. Delayed test showed greater improvement in accuracy after sleep compared to wake ($t(18) = 2.795, p=.012$), no differences in distance or vector. Median split by Immediate test performance revealed that initially lower performance showed the greatest improvement after delay in the sleep group ($t(18) = 2.818, p = .011$,

but not the wake group ($t(18) = -1.051, p = .308$). Additionally, these same subjects' vector direction was initially worse at Immediate Test ($t(18) = -2.9, p = .01$), and improved with sleep, becoming equivalent to the better performers at Delay test ($t(18) = -.336, p = .74$).

Conclusion: We demonstrate a novel spatial navigation/memory tasks using Minecraft that shows sleep-dependent learning across two distinct environments. We showed enhancement of spatial location accuracy after a night of sleep compared to wake. We further demonstrate that with sleep, those with worse initial performance show the greatest memory and navigation improvement, consistent with other findings that sleep supports enhancement of weaker memories and extended to the spatial-domain. This novel platform can be used to evaluate spatial memory across the lifespan and within special clinical populations.

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056

EFFECTS OF SIMULATED SHIFT SCHEDULES ON VISUAL SEARCH

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Introduction: Visual search is important in many operational tasks, such as passive sonar monitoring in naval operations. Shift work can contribute to fatigue and task performance impairment; in particular, backward rotating shift schedules have been shown to impair vigilant attention performance. However, the impact on visual search performance, above and beyond impaired vigilant attention, is unknown. We investigated the effects of two distinct shift work schedules using a visual search task with properties of real-life visual search performance.

Methods: N=13 adult males (ages 18–39) completed a 6-day/5-night laboratory study with an acclimation day, four simulated shift days, and a recovery day. Shift days involved either a 5h-on/15h-off backward rotating schedule (n=8) or a 3h-on/9h-off fixed schedule (n=5). The visual search task was performed once per shift at varying time of day depending on shift. Participants viewed search arrays where stimuli consisted of colored letters of different shapes. Over three trial blocks of 24 trials each, participants determined if a target was present or absent among 1, 5, 15, or 30 distractors. Similarity between targets and distractors was manipulated between blocks, such that targets differed from distractors by color only, shape only, or either color or shape but not both. For each distinct target feature block, and separately for presence or absence of a target, slopes of response times regressed against number of stimuli were calculated to quantify visual search rates. Mixed-effects ANOVA was used to analyze visual search rates by shift schedule and shift day.

Results: There were no significant effects of shift schedule (all $p>0.30$), shift day (all $p>0.13$), or their interaction (all $p>0.22$) on visual search rates.

Conclusion: Previous work showed degraded vigilant attention in the shift schedules considered here, especially in the backward rotating schedule, which may compromise operational performance. However, while our sample may have been too small to have adequate statistical power, we failed to identify specific impairments in visual search with statistical significance. It remains to be determined whether greater levels of fatigue, such as could be induced by total sleep deprivation, would reveal significant visual search deficits.

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057

AGE-RELATED CHANGES IN SLEEP IMPACT LEARNING-RELATED FUNCTIONAL CONNECTIVITY IN THE CORTICO-STRIATAL-HIPPOCAMPAL SYSTEM

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Introduction: Older adults do not consolidate newly learned motor sequences with the same efficiency compared to younger adults, and there is evidence that enhanced consolidation by sleep is also impaired with age. It is known that brain activity in the hippocampal-cortical-striatal network is important for off-line consolidation of motor-sequences, however, the intricacies of how communication within this network is altered by sleep in order to facilitate consolidation is not known.

Methods: In this study, 37 young and 49 older individuals underwent resting state MRI before training on a MSL task, as well as after training, and then once again, after either a nap or a period of awake rest.

Results: Preliminary analysis showed a significant difference in functional communication (FC) in the hippocampal-cortical-striatal network, with younger subjects showing increased FC compared to younger individuals. Follow-up analyses revealed this effect was driven by younger subjects who showed an increase in FC between striatum and motor cortices, as well as older subjects who showed decreased FC between hippocampus, striatum, and precuneus. Therefore, an opposite effect of sleep was observed in younger vs. older participants, where young participants primarily showed increased communication in the striatal-motor network and older participants showed decrease in key nodes of the default mode network.

Conclusion: This shows that changes to sleeps' ability to optimize functional communication may disrupt sleep-enhanced MSL consolidation in old age.

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058

THE INTERACTIONS OF SLEEP, HEART RATE VARIABILITY AND AGING ON AN EMOTIONAL DIRECTED FORGETTING MEMORY TASK

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Introduction: The ability to forget information plays an important role in our daily lives. Sleep plays a role in memory formation and as we age, sleep-quality and memory decrease. For emotional memory a drop in preference for negative stimuli is presented with aging. Heart-rate variability (HRV), a measurement of cardiac autonomic-activity, has been related to cognitive processes. It is unknown how HRV impacts sleep-dependent memory updates in older adults. Here, we investigated HRV and sleep-related emotional memory updates in the context of aging using a Directed-Forgetting (DF) paradigm.

Methods: We tested younger [N=105,18-25yr] and older adults [N=119,60-85yr]. Subjects encoded a DF Word-Paired task, in which either negatively/neutral-valenced word-pairs were cued

to-be-remembered (Retain) or forgotten (Alter) for a later test. They then took a polysomnographically-recorded (PSG) nap including HRV. Next, recognition was tested. Memory for both Retain and Alter words was measured. We compared memory, sleep-quality measured by Sleep-Efficiency (SE) and HRV, measured by normalized High-Frequency (HFnu), an indicator of parasympathetic activity. Bivariate correlations were used to measure the associations.

Results: Younger adults showed greater performance on both Retain and Alter word-pairs ($p < .001$) with being able to better forget Alter word-pairs only for the negative-condition ($p < .001$). Younger adults had a higher SE ($p < .001$) and a higher HRV-HFnu in both Stage2 ($p = .02$) and Stage3 ($p = .03$). Only for older adults in the neutral-condition, we found correlations between memory and sleep [Retain: $r(20) = .52$, $p = .01$; Alter: $r(20) = .51$, $p = .01$]. Finally, among younger adults, in Stage 2, memory was related to HFnu for both neutral [Retain: $r(17) = .46$, $p = .05$] and negative-condition [Retain: $r(25) = -.41$, $p = .03$; Alter: $r(25) = -.39$, $p = .05$]. No correlations were found for older adults (all $ps > .11$).

Conclusion: Our result indicate a possible loss of the ability to intentionally forget irrelevant information among older adults and a role for the saliency to forget irrelevant items among younger adults. In addition, aging brain may benefit from sleep only for the neutrally-valenced items; the memory biased seen in aging. Finally, for younger adults HRV may be related to memory updates and its role depends on specific sleep stages however this association is faded away with aging.

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